REMARKS

Claims 1, 37, 38, 40, 41, 43-45, 54-56 and 58-62 are pending in the application and all claims are rejected.

Claims 70 and 71 are added as new dependent claims. Support is found, for example, at page 33, lines 17-21 and page 36, lines 2-5. No new matter is presented.

Claims 1, 37-38, 41, 43-45, 54-56 and 59-62 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Wong et al. (US 2002/0156067, already of record) and Jordan et al. (US 2002/0173513) further in view of Harvey et al. (reference already of record) as evidenced by Owens et al (reference already of record).

In addition, claims 40 and 58 is rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Jordan et al., Wong et al. and Harvey as evidenced by Owens et al as applied to claims 1, 37-39, 41, 43-45, 54-56 and 59-62 above, and further in view of Bando et al (US 2004/0058935, PCT filing date of Sept 25, 2002.

Applicants respectfully traverse the rejections for the reasons of record and for the following additional reasons.

It is submitted that the cited references, taken alone or in combination, do not fairly teach or suggest the claimed invention.

As previously pointed out and as acknowledged by the Examiner, the primary reference, Wong et al, does not specifically teach a composition or method comprising aripiprazole and citalopram or escitalopram as presently claimed.

The Examiner asserts that citalopram and escitalopram are functionally equivalent to venlafaxine based on the teachings of Harvey et al and Owens et al and therefore it would have

been obvious to arrive at the claimed invention based on the combined teachings of the references.

Applicants respectfully disagree and submit that citalopram and escitalopram are not functional equivalents of venlafaxine. It is submitted that venlafaxine, which acts both on serotonin and norepinephrine, has been reported as having superior effects compared to selective serotonin reuptake inhibitors, such as citalopram or escitalopram. Applicants refer to the following scientific journals submitted with the response filed August 17, 2010, supporting such position:

> (1) British J. Psychiatry (2001) 178, 234-241 describes on page 234, Conclusions and lines 24-30 of the middle column that venlafaxine, which is an SNRI, is significantly superior to SSRIs in terms of remission rates.
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> (2) British J. Psychiatry (2001)[1] 180, 396-404 describes on Conclusions and Clinical Implications on page 404, that venlafaxine has greater efficacy than SSRIs.
>
> (3) Biol. Psychiatry (2002)[2] 52, 1166-1174 describes on Conclusions that venlafaxine is significantly more effective than SSRIs in improving depression, perhaps due to the enhancing both serotonin and norepinephrine.

Accordingly, it is submitted that one of ordinary skill in the art would not consider venlafaxine as a functional equivalent to escitalopram and citalopram, which are selective serotonin reuptake inhibitors, and thus one of ordinary skill in the art would not arrive at the claimed invention.

For at least the foregoing reason, it is submitted that the claimed invention is not obvious in view of the cited art.

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[1] The journal was published in May 2002 as evidenced with "1 Periodical Search Results" previously submitted with the Response filed August 17, 2010 submitted herewith.

[2] Please note that said journal was published on December 15, 2002 as evidenced with "Archive of 2002 on line issues" previously submitted with the Response filed August 17, 2010.

Moreover, it is submitted that the claimed invention provides synergistic effects, which are completely unexpected from the cited references.

The Examiner asserts that aripiprazole has been shown to have additive or synergistic effects in the treatment disorders of central nervous systems such as depression when combined with serotonin reuptake inhibitors (Wong et al) and as such, it is not unexpected that aripiprazole also shows a synergistic effect when combined with citalopram or escitalopram.

Applicants respectfully disagree.

It is submitted that Wong et al formalistically discloses the concomitant use of aripiprazole with duloxetine, venlafaxine or milnacipran as one of the combinations. However, Wong et al fails to include any teachings or suggestions regarding the effects of said combinations whatsoever.

In general, it is difficult to predict effects in the field of pharmaceuticals; despite the Examiner's assertion that the above mentioned combinations would have synergistic effects, one of ordinary skill in the art can hardly predict the effects achieved by the concomitant use of aripiprazole with duloxetine, venlafaxine or milnacipran. Indeed, it is even more difficult to predict whether the concomitant use of aripiprazole with citalopram or escitalopram, which the present inventors for the first time discovered, would have synergistic effects.

In addition, it is submitted that the closest prior art combinations are those specifically disclosed in Wong et al., i.e., clozapine, olanzapine or risperidone with reboxetine (EXAMPLES 1 and 2), which combinations are those of a selective norepinephrine reuptake inhibitor (reboxetine) and a neuroleptic drug, rather than the combinations of aripiprazole with duloxetine, venlafaxine or milnacipran. That is, there is no specific teaching in Wong et al. regarding the combination of aripriprazole with duloxetine, venlafaxine or milnacipran, and thus based on the

disclosure of Wong et al., one of ordinary skill in the art would not have expected the effects achieved by such combination as demonstrated in the Declaration submitted on March 18, 2009. Thus, it is submitted that requiring a comparison of the claimed invention to a combination of aripiprazole with duloxetine, venlafaxine or milnacipran is based on improper hindsight.

As demonstrated, the present concomitant use (aripiprazole and citalopram or escitalopram) clearly shortens the prolonged immobility time in the forced swimming test of mice and tail suspension test (indicating that they have anti-depression effects), and have a synergistic effect. In other words, the concomitant use of aripiprazole and citalopram or escitalopram reduces the administration dosage for each drug, leading to lower side-effects and is excellent in safety. On the other hand, the concomitant use described in Wong et al, (risperidone, olanzapine or clozapine and reboxetine) did not significantly shorten the prolonged immobility time in the forced swimming test of mice (indicating that they tend to deteriorate).

In summary, Wong et al does not disclose nor suggest the inventive combination or the advantageous effects of the present invention at all.

It is noted that citalopram and escitalopram are not even mentioned, let alone compared with venlafaxine, in the primary references, and are different in their effects as discussed above. Thus, citalopram and escitalopram are far from being equivalents of venlafaxine.

In view of the above, it is submitted that the present invention is patentable over the cited art for these additional reasons. New claims 70 and 71 are patentable by virtue of their dependency.

Accordingly, Applicants respectfully request withdrawal of the §103 obviousness rejection.

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

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23373
CUSTOMER NUMBER

Date: March 28, 2011